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From: "Fred Henretig MD" <henretig@email.chop.edu>

To: lederberg@mail.rockefeller.edu Cc: edward.eitzen@det.amedd.army.mil

Subject: Re: riposte to Sidel

Dear Dr Lederberg - it's been 2 mos and you may have long forgotton about the submission to AJPH of a rejoinder to the Cohen, Sidel editorial Nov, '99. We've been waiting all this time to hear from them as to whether they would even consider the full, or nearly so, text, or would insist on a short letter to the editor. I've just received late last week a response- our commentary is accepted in full, to be packaged in their section called "On the other hand". This format allows a full editorial length counter-editorial to a previously written piece, with an adjacent "response" from the original editorialists. An example (on managed care issues) is in the June 2000 issue, p 984-6. This format would of course allow Sidel et al the "last word", but AJPH readers could at least read 2 sides of the argument side by side. I'm still for it, and have sent my revised ms, which includes your very appreciated comments (and title suggestion!), to Ed Eitzen's group at USAMRIID to look over. Needless to say, we'd be honored to have you join in as a co-signatory, if the ms met your standards and you were so inclined. I'm attaching the revision, both for you to consider the above, or even to say if I included your comments accurately, and whether you feel any additional work is necessary. I tried to make this version a little less confrontational and more of an independent opinion piece responding to general criticisms of the national domestic preparedness plan, rather than purely a critique of the Nov Cohen/Sidel commentary. Thank you very much in advance, Fred

Biodefense: Hand-in-hand with Public Health Recent commentaries on bioterrorism and public health in the Journal (1) and elsewhere (2) have challenged the necessity of a robust government-funded bioterrorism defense strategy, undue publicity and media hyperbole (3), and in particular the partnering of civilian and military medical experts in coordinating domestic preparedness in this arena (1,2). Similar arguments have been expressed in media publications (4). While we agree with many of the individual principles cited in these discussions, we believe that bioterrorism does indeed pose a serious public health and security threat to our nation. Further, it is our conviction that cooperation between a broad array of government agencies, both military and civilian, as well as with concerned academic and professional organizations, is precisely the correct approach for addressing this potential national catastrophe, while enhancing our public health infrastructure's capabilities to address new or re-emerging natural infectious disease outbreaks.

We can begin by noting major areas of agreement with several core principles contained in the critiques of biodefense strategy (1), but offer a somewhat differing interpretation in the application of these principals. First, it has been observed that the US government's bioterrorism initiatives might strengthen public health practice, particularly with improved infectious disease surveillance programs, which will enhance the recognition and control of emerging infectious diseases. We agree, and further note the enormous potential for such a positive impact to result in one of this era's major advances in public health infrastructure, at a time when funding for public health is otherwise diminishing (5). Second, the issue of cost, and lost funding for other critical public health programs, has been raised. While it is true

that the Departments of Health and Human Services (HHS) and Defense (DOD) counter-bioterrorism funding has increased significantly in the past few years, these still represent small fractions of HHS and DOD overall budgets. Public health should not be a zero sum game. When health crises arise (as was the case with the AIDS epidemic), overall funding must be increased within our society's limits. In our view, the potential threat of bioterrorism to national health interests mandates considerable funding. This in no way suggests a desire to decrease funding for other worthy public health initiatives. We too, for example, urge increased support and funding for fighting the re-emergence of tuberculosis in our inner cities, expanded childhood vaccination programs, efforts to counter-act increasing antibiotic resistance, and enhanced infectious disease surveillance efforts at local and national levels.

Third, it has been suggested that the US holding back from unilateral general and complete disarmament (GCD) in its nuclear weapons policy plays a role in motivating weapons of mass destruction proliferation on the part of other nations. We do not enter that debate here, nor wish to discuss in depth the implications of the US deciding to adopt GCD. The fact remains we face a world in which biologic weaponry is being more widely adopted, in the face of the Biologic Weapons Convention (BWC), which appears far more difficult to verify or enforce than nuclear non-proliferation treaties. For example, there is no doubt that after the US unilaterally denounced offensive bioweapons use in 1969, the former Soviet Union used this window of opportunity to accelerate their biowarfare research and development in the 1970s and 1980s (6). We fervently oppose proliferation of all weapons of mass destruction, and expect that virtually all medical scientists and physicians, both civilian and military, would so agree. Biodefense programs may reduce the pressure to brandish our nuclear strength as our only means of deterring biological attack. Finally, in this regard, rational calculations of national defense strengths and weakness and corresponding decisions about weapons strategy hold little relevance to the possibility of fanatical domestic or foreign terrorists attacking our civilian population with bioweapons (5). Fourth, the biodefense critique notes that expanded bioterrorism defensive efforts may contain an inherent potential for covert offensive biological weapons use or research. It is reported that numerous biomedical researchers, including many members of the National Academy Sciences (NAS), recently signed a pledge to not engage in research or teaching that might further the development of chemical or biological weapons. We agree completely with this position, which has been official US policy for over 30 years. Of note, the NAS is now participating vigorously in counter-terrorism domestic preparedness efforts. The Institute of Medicine of the NAS recently released a 279-page committee report that stresses the importance of integrating domestic preparedness for chemical or biological terrorism within existing emergency medical services (EMS) and public health agencies, and delineated numerous recommendations for high priority research and development needs to prepare optimally for this threat. (7) The IOM committee consisted of 17 national experts drawn primarily from civilian academic and public health institutions, and the report was further reviewed by eight distinguished, independent reviewers. Other opinions have been expressed by critics of bioterrorism defense planning with which we more fully disagree. It has been suggested that further bioterrorism initiatives are questionable and should be examined in light of potential necessity, efficacy, safety and cost (1). The issue of cost has been touched upon already, so that our remaining remarks will address the first three of these concerns. As to necessity, critics have commented that stockpiles of biological weapons are only "allegedly" maintained

by several nations, implying this might not be the case, and that the ability to weaponize biological agents is "externely limited," so that the risk of such an attack by terrorists is small. In our view, there is overwhelming evidence of recent biological weapons stockpiling, particularly in Iraq, as determined unequivocally at the time of the Gulf War and by subsequent United Nations Special Commission investigations (8), and in the former Soviet Union, as per revelations from disaffected scientists from the Soviet bioweapons program. (6) Regarding the technical difficulty of producing bioweapons, it is likely true that a bioterrorism incident involving wide-spread dissemination of a highly lethal agent such as anthrax over a large metropolitan area might require the sophistication and resources of a state-sponsorship, and thus be considered a "low-probability, high consequence event." (9) However, many public health, national security and military authorities consider that even such a low probability event, given the difficulty in quantifying just how low the probability, and its attendant potential for catastrophic consequences, is worthy of preparation.(5,7,9) Of perhaps greater concern, a smaller scale attack that might "only" sicken thousands and kill hundreds is far more likely, and well within the capacity of "amateur" terrorists. For example, in 1984 in the Dalles, OR, 751 people developed salmonellosis, with 44 requiring hospitalization, after the intentional spread of bacteria on salad bars in order to disrupt a local election (10). An incident with a more lethal agent might have resulted in far greater morbidity, and consequent mortality, as illustrated by the accidental release of airborne anthrax in 1979 in Sverdlovsk, USSR, resulting in at least 66 deaths (11). Are we ready to accept even such a "lesser" disaster without attempting to formulate strategies to mitigate the potential After the bombings of the World Trade Center in New York and the federal building in Oklahoma City, and the sarin attack in Tokyo, does anyone really believe that individuals or organizations do not exist today with the motivation to attack innocent civilians with biological weapons, if they have that capability? We have found little actual discussion in the biodefense critique regarding potential efficacy of the bioterrorism preparedness programs currently funded or proposed. The main concern posited is that these initiatives are "reminiscent of the civil defense programs promoted*during the Cold War * [that fostered] the delusion that nuclear war was survivable" (1). We believe this to be an inaccurate analogy. Nuclear war in the context of the US and USSR exchanging massive numbers of ballistic missiles carrying nuclear weapons would by all accounts have resulted in holocaust. This is not the scenario envisioned by national public health, security, and military experts in the context of bioterrorism. Hundreds, perhaps thousands of casualties are likely. The consequences on the public's health would be catastrophic with the loss of many innocent lives; however, the overall infrastructure of society would hopefully remain intact. We can mitigate considerably the severity of such a catastrophe, and certainly its spread in the context of contagious agents, by careful, cost-effective training and consciousness-raising of the EMS and medical communities, as is being currently initiated. (12) Early recognition of a terrorist attack, plans to respond, and modest stockpiles of drugs can ameliorate some of this impact. Vaccines might also play a role, primarily in the context of smallpox. Unfortunately, the public health triumph of globally eradicating smallpox in 1980, and the subsequent discontinuation of vaccination unknowingly opens the door for its possible use as a terrorist weapon. The epidemic, even pandemic, potential which we know resides in the smallpox virus means we must have stockpiles of vaccine to control the spread of this virus should it be used (13). Further advances in early detection and identification of bioagents, and in immunization and therapeutic modalities will enhance our response capability (and have obvious dual-use applications in our approach to ordinary, natural infectious diseases). I to take these steps

would constitute a massive "malpractice" error of omission on the part of public health and medical authorities. The safety issue regarding bioterrorism initiatives constitutes a major issue addressed by recent critics of biodefense preparedness (1). Several concerns are cited, most reflecting in one capacity or another, a distrust of "militarism" in the national agenda on bioterrorism. We offer some differing views on these concerns. First, examples are cited of the former US offensive bioweapon program activities, from the era before the Biological Weapons Convention which, from the perspective of 2000, might seem excessively militaristic. In fact, that era was shaped considerably by consensus civilian and military Cold War thinking, and predated modern concepts of informed consent in medical research. Many research policies in academic medical and civilian public health spheres from that era would not stand up to current ethical standards (e.g., the Tuskegee syphilis study). Since 1969, the US has conducted only defensive efforts in the arena of biological weapons. (14) Research at institutions such as the US Army Medical Research Institute of Infectious Diseases is conducted under scrupulous attention to informed consent and existing Freedom of Information Act policy, and its results are published in peer-reviewed medical and scientific literature. Most of the expertise in considering the consequences of biological warfare attack has obviously been based historically in military medical institutions charged with providing optimal protection from and treatment for such an attack upon our country's soldiers under battlefield conditions. In the context of current events, with the emerging threat of terrorist use of biological weapons on civilian populations, it is natural for EMS and public health agencies like the Office of Emergency Preparedness and Centers for Disease Control and Prevention (CDC) to partner with military medical sources of expertise in planning for potential civilian mass casualty incidents resulting from bioterrorism. There are ample precedents for the advancement of civilian public health and general medical practice as a consequence of government-funded research and training prompted by national security or defense concerns. The highly regarded Epidemic Intelligence Service of the CDC was organized in the 1950s precisely as a response to our country's then perceived vulnerability to biological warfare attack from Cold War antagonists (11,15). Many modern emergency medical practices, trauma and burn care, and vaccines are derived from military medicinebased research, battlefield treatment, and evacuation experience. Numerous current initiatives enhancing medical and public health practice at the local and regional levels will ultimately add considerably to our ability to respond effectively to natural infectious disease emergencies and unintentional hazardous materials incidents, thanks to training undertaken in the context of biological (12) and chemical (16) terrorism preparedness. Biodefense critics further decry the evolution of Defense Advanced Research Projects Agency (DARPA) funding for defensive biological weapon-related research at civilian academic medical centers. This is hard to understand. DARPA funds projects proposed by academic medical scientists at many of our nation's leading medical institutions, many of which will have considerable "spin-off" for addressing problems of emerging natural infectious diseases. (17) DARPA*funded research has an enviable track record in such spin-off potential for the benefit of civilian technology. Witness its seminal research into a defense-related computer network that has since evolved into the global phenomenon and economic engine known as the Internet. In conclusion, we find much to value in current domestic preparedness efforts in the realm of biological terrorism, and in particular, toward shared efforts by military medical and civilian public health agencies in working together to defend the American public against this potential national security and consequent public health catastrophe. We found some irony in the juxtaposition of the Journal's recent commentary regarding the celebration of the APHA's first century of progress in public health (18) to the editorial critiquing current national biodefense policy (1). Almost 100 years ago, at the APHA meeting in Indianapolis, Oct 22-26, 1900, a young medical scientist presented a landmark report on yellow fever, linking this dreaded epidemic disease to mosquito transmission. This work paved the way for its virtual eradication from the US and most industrialized societies through the application of basic, modern public health principles. We refer, of course, to Dr. Walter Reed, a surgeon in the US Army Medical Corps (19). We find ample historical precedent for the benefits of linking public health support with issues of national security, as have others (5). We consider that such a linkage can have critical dual-use benefits in protecting our nation from bioterrorism as well as emerging and re-emerging natural infectious outbreaks, and in the process provide a broad base of social and political support for strengthened and increased funding for our national public health infrastructure.

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REFERENCES

REFERENCES

- 1. Cohen HW, Gould RM, Sidel VW. Bioterrorism initiatives: public health in reverse? Am J Public Health 1999; 89:1629-1631.
- 2. Cohen HW, Sidel VW, Gould RM. Prescriptions on bioterrorism have it backwards (letter). BMJ 2000; 320:1211
- 3. Cole LA. Risks of publicity about bioterrorism: anthrax hoaxes and hype. AJIC Am J Infect Control 1999; 27: 470-473.
- 4. Vergano D. Bioterrorism under fire. USA Today, June 21, 2000.
- 5. Guidotti TL. Bioterrorism and the public health response. Am J Prev Med 2000; 18:178-180.
- 6. Alibek K. Biohazard. Random House, New York, 1999.
- 7. Institute of Medicine-National Research Council. Chemical and biological terrorism: research and development to improve civilian medical response. National Academy Press, Washington, D.C. 1999.

- 8. Zilinskas RA. Iraq's biological weapons: the past as future? JAMA 1997; 278: 418-424.
- 9. Tucker JB. National health and medical services response to incidents of chemical and biological terrorism. JAMA 1997; 278: 362-368.
- 10. Torok TJ, Tauxe RV, Wise RP et al. A large community outbreak of salmonellosis caused by intentional contamination of restaurant salad bars. JAMA 1997; 278: 389-395.
- 11. Franz DR, Jahrling PB, Friedlander AM et al. Clinical recognition and management of patients exposed to biological warfare agents. JAMA 1997; 278: 399-411.
- 12. Eitzen EM Jr. Education is the key to defense against bioterrorism. Ann Emerg Med 1999; 34:221-223.
- 13. Henderson DA, Inglesby TV, Bartlett JG et al. Smallpox as a biological weapon-medical and public health management. JAMA 1999; 281: 2127-2137.
- 14. Christopher GW, Cieslak TJ, Pavlin JA, Eitzen EM. Biological warfare: a historical perspective 1997; 278;5:412-417.
- 15. Langmuir AD, Andrews JM. The Epidemic Intelligence Service of the Communicable Disease Center. Am J Public Health 1952; 42:235-238.
- 16. Brennan RJ, Waeckerle JF, Sharp T, Lillibridge SR. Chemical warfare agents: emergency medical and emergency public health issues. Ann Emerg Med 1999; 34:191-204.
- 17. Stephenson J. Pentagon-funded research takes aim at agents of biological warfare. JAMA 1997; 278:373-375.
- 18. Fee E, Brown TM. A century of progress in public health? Am J Public Health 1999; 89:1627-1628.
- 19. Reed W, Carroll J, Agramonte A. The etiology of yellow fever: an additional note. JAMA 1901; 36: 431- 440